SCANCELL

AT THE FOREFRONT OF IMMUNO-ONCOLOGY

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February 2020

LSE: SCLP.L

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SCANCELL IS OPERATING AT THE FOREFRONT OF IMMUNO-ONCOLOGY

THE MARKET

- Expected to exceed US$100bn p.a. by 2022 (source: ResearchAndMarkets.com 30 November 2018)
- Merck and BMS have developed blockbuster checkpoint inhibitor drugs with sales > US$7bn p.a.
- Checkpoint inhibitors prevent tumour cells supressing the immune system
- Biopharma companies worldwide are making huge investments to enter the I-O market

THE OPPORTUNITY

- Checkpoint inhibitors are applicable only to a minority of cancer patients
- The race is on to find new approaches for complementary therapies to increase the eligible patient population
- Scancell's **IMMUNOBODY®** , **MODITOPE®** **and AvidiMab™** platforms have broad applicability

CLINICAL STAGE ASSETS

- Four lead products in development
- Phase II study initiated and Phase I/II studies in preparation targeting multiple cancer indications

SCANCELL

- Scientific founder Prof. Lindy Durrant
- 23 employees based in Oxford and Nottingham (12 PhDs)
- AIM quoted (SCLP)

OUR PARTNERS

BIONTECH · CANCER RESEARCH UK · The University of Nottingham · ISA Pharmaceuticals · ichor medical systems

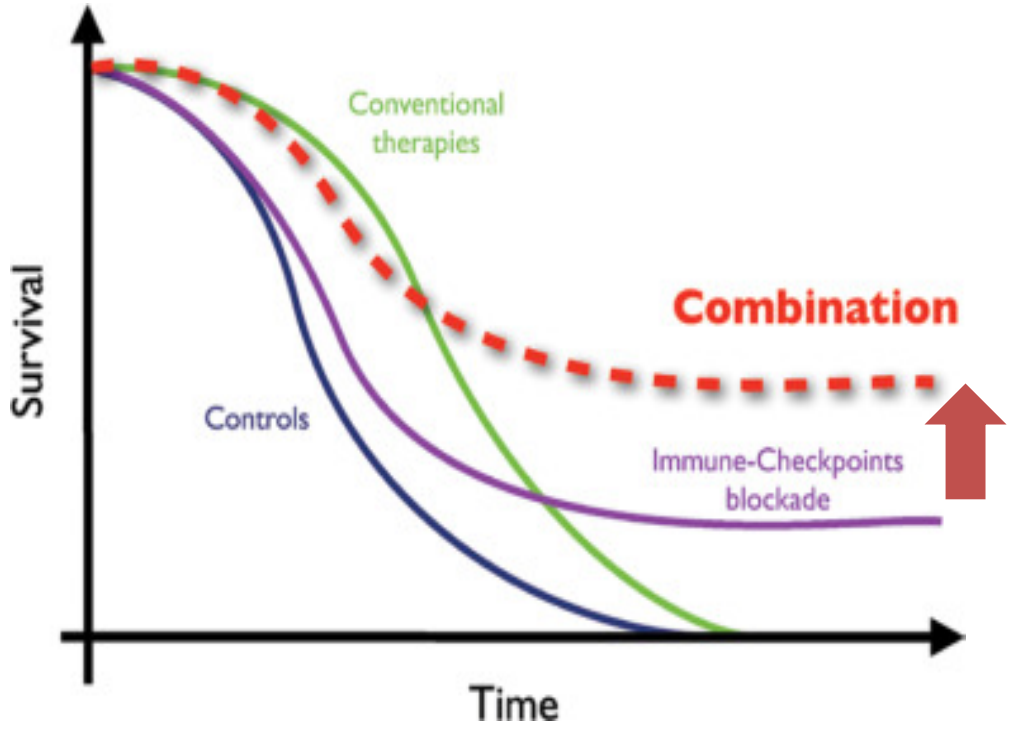
3 PLATFORMS, 4 LEAD PRODUCTS + MULTIPLE CANCER INDICATIONS

IMMUNO ONCOLOGY DEVELOPMENT & COMMERCIAL DRIVERS

- Innovative platform technologies to generate novel therapeutics
- Validation through translation of core science to clinically relevant data
- Unmet need: response rates and duration of response to checkpoint inhibitors vary greatly depending on the type of cancer
- Growth and uptake of new immunotherapies will be based on incremental clinical value beyond SoC

The future of immuno-oncology is in novel combination therapies and new modalities that:

- Address the unmet needs in hard to treat cancers
- Provide an increased and durable response
- Do not increase toxicity
- Do not significantly increase overall cost of treatment



DEVELOPMENT PIPELINE

IMMUNOBODY®

- **SCIB1:** Targets malignant melanoma. Phase 2 trial in patients receiving immune checkpoint inhibitor
- **SCIB2:** Targets solid tumours. Phase 1/2 trial with immune checkpoint inhibitor to be funded and sponsored by Cancer Research UK (CRUK)

MODITOPE®

- **Modi-1:** Phase 1/2 trial including breast, ovarian, renal and head & neck cancer planned for 2H'20
- **Modi-2:** Targets multiple solid tumours
- **TCR collaboration:** To clone and characterise T cell receptors (TCR) against Modi-1 specific epitopes

AvidiMab™ / TaG mAbs

- **Anti-glycan mAbs:** Monoclonal antibodies (mAbs) targeting tumour associated glycans (TaGs)
- **AvidiMab:** Broad potential for enhanced potency of mAbs
- **Research collaboration:** Evaluation in other platform technologies/formats

	Lead Candidates	Preclinical	Phase 1/2	Phase 2
ImmunoBody	SCIB1 Late stage melanoma		Completed	Phase 2 trial with checkpoint inhibitor
ImmunoBody	SCIB2 Solid tumours e.g., non-small cell lung cancer (NSCLC)		Phase 1/2 trial with checkpoint inhibitor	
Moditope	Modi-1 Triple -ve breast (TNBC), ovarian, renal, head & neck (HNSCC) cancers		Phase 1/2 trial	
Moditope	Modi-2 Anti-solid tumours	Preclinical validation		
Moditope	Moditope TCR characterisation	BIONTECH		
mAbs	Tumour associated glycans (TaGs); Multiple solid tumours	Preclinical validation	The University of Nottingham	

CANCER RESEARCH UK

SCANCELL'S CANCER VACCINE PLATFORMS

- Key challenge is to stimulate an effective T cell response to reject or kill the growing tumour
- Most vaccine strategies only stimulate low frequency, low avidity T cell responses that fail to control tumour growth
- Scancell's novel therapies stimulate high avidity CD8 and/or CD4 T-cells that efficiently kill tumours

IMMUNOBODY®

- DNA-based platform generates high avidity CD8 T-cells by presenting T-cell epitopes of known cancer antigens through a unique dual mode of action

MODITOPE®

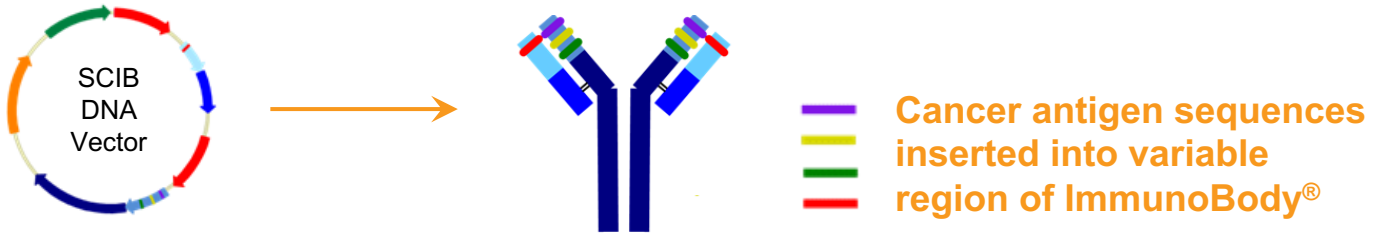
- Modified peptides that generate potent killer CD4 T-cells to target antigens induced by stress-induced post-translational modifications (siPTM vaccines)

Clinical and pre-clinical studies indicate:

- Favorable safety profile in patients (SCIB1)
- Potential to address the unmet needs in hard to treat cancers
- Provide an increased and durable response
- Low cost of goods compared to cell therapies

THE IMMUNOBODY® PLATFORM

- Proprietary patent protected platform
- Several cancer associated T cell epitopes are engineered into a human antibody framework to make a genetic antigen/antibody complex



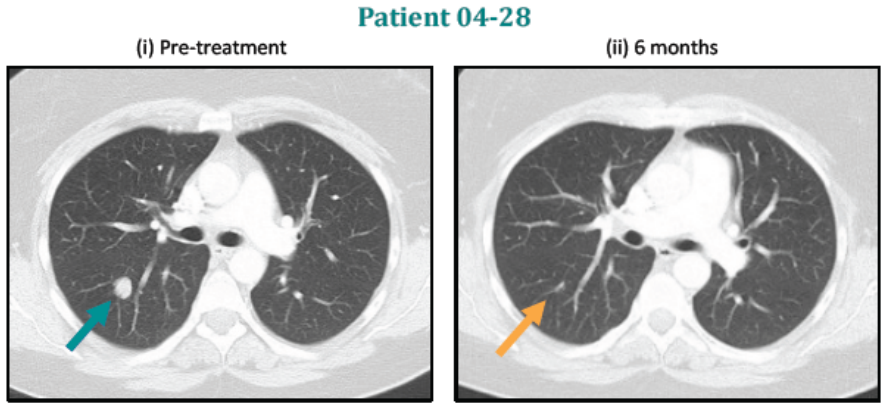
- Novel dual mechanism of action based on **direct** and **cross-presentation**
- SCIB1 for melanoma (**TRP-2/gp100 melanoma associated antigens**): Phase 1/2 clinical trial complete, Phase 2 study in combination with pembrolizumab underway
  - delivered as a DNA plasmid using electroporation
- SCIB2 for solid tumours (**NY-ESO-1**): Clinical development partnership with CRUK
  - nano-particle delivery evaluated as an alternative mode of delivery

SCIB1 IN PATIENTS WITH LATE STAGE MELANOMA

SCIB1 has an excellent safety profile with no dose-limiting toxicities and no serious adverse events related to study drug or delivery device

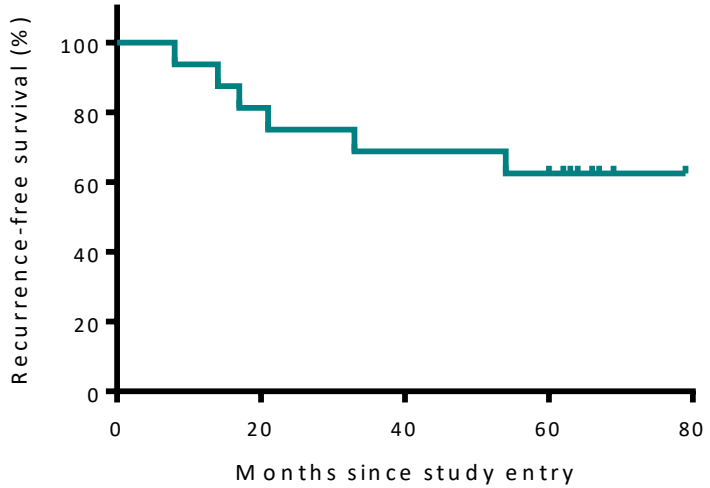
TUMOUR RESPONSE

Patient with tumour received 8 mg SCIB1 and showed a marked reduction in size of detectable lung lesions

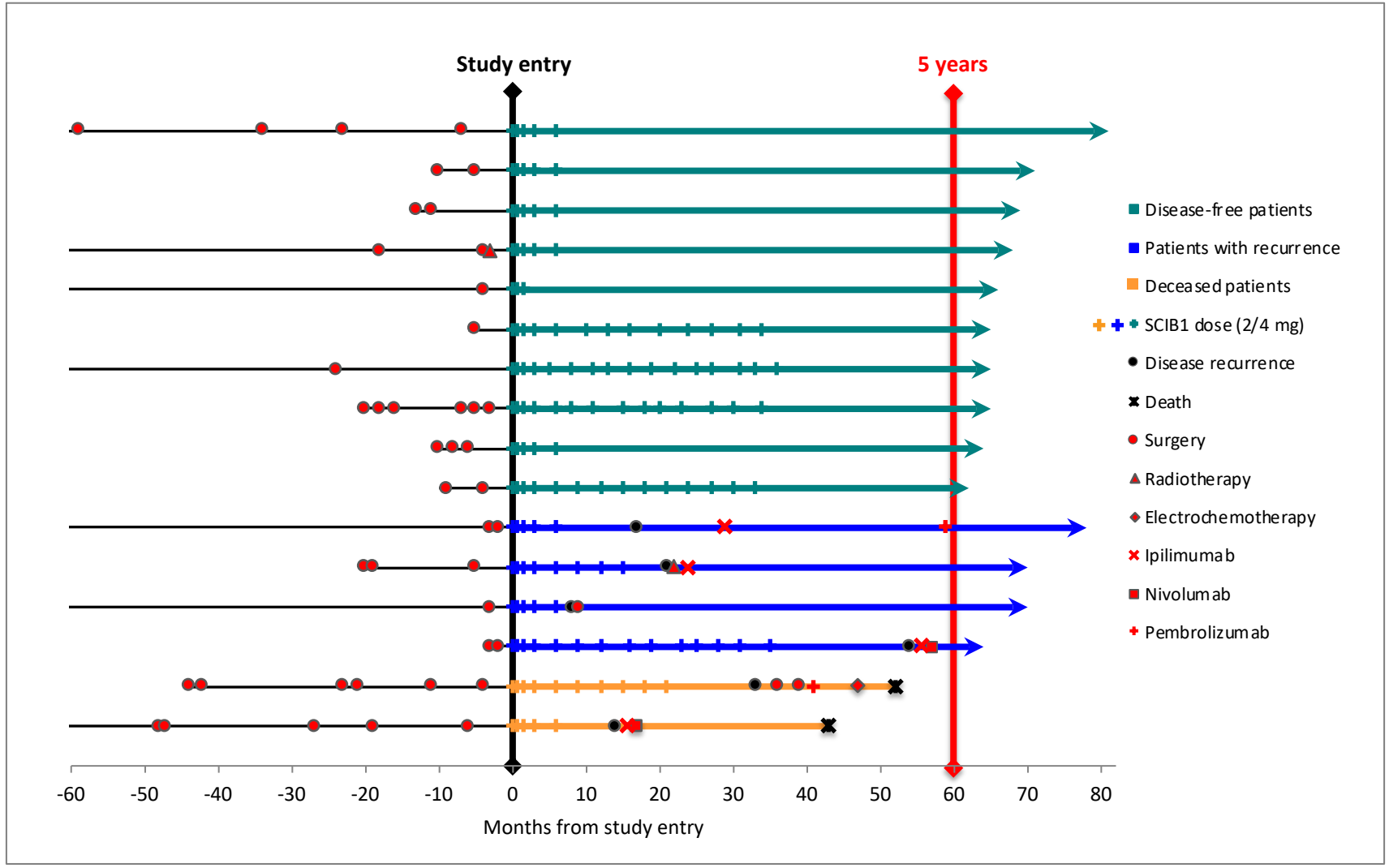


SURVIVAL IN RESECTED PATIENTS

- Overall survival with SCIB1 treatment superior to historical survival rates
- 14 of 16 resected patients receiving 2-4 mg doses have survived for more than 5 years (February 2018)
- Melanoma recurrence rates are lower in SCIB1-treated patients than historical controls



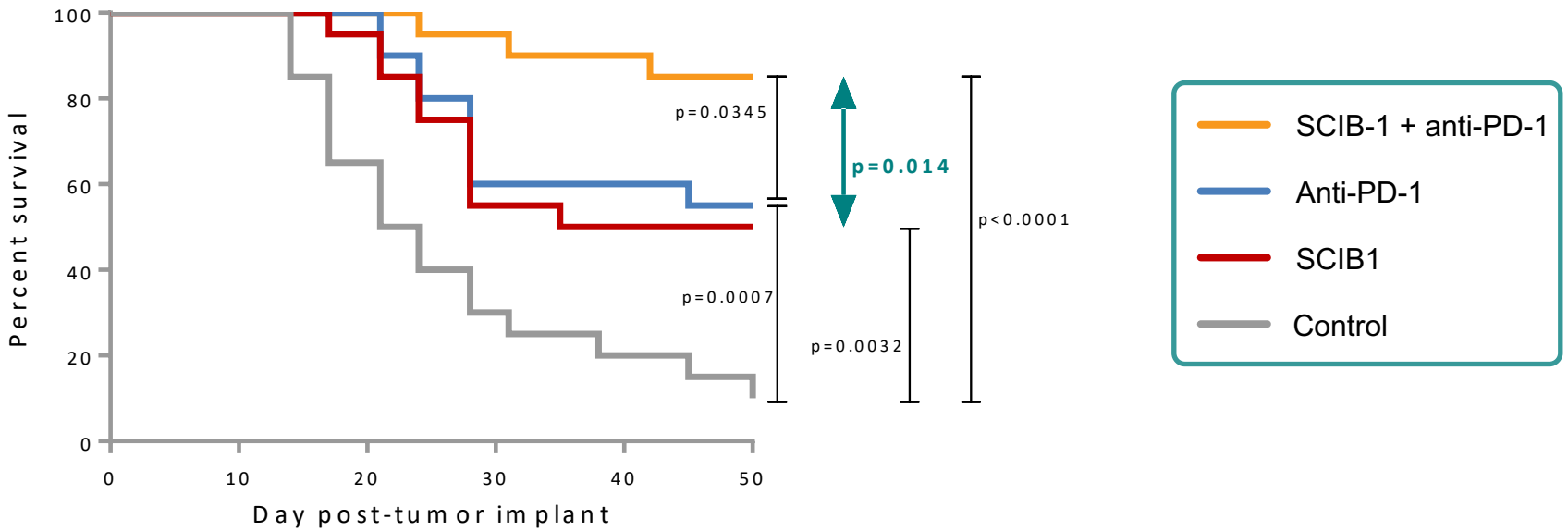
PATIENTS WITHOUT TUMOUR PRESENT AT STUDY ENTRY



SCIB1 BOOSTS IMMUNE CHECKPOINT THERAPY

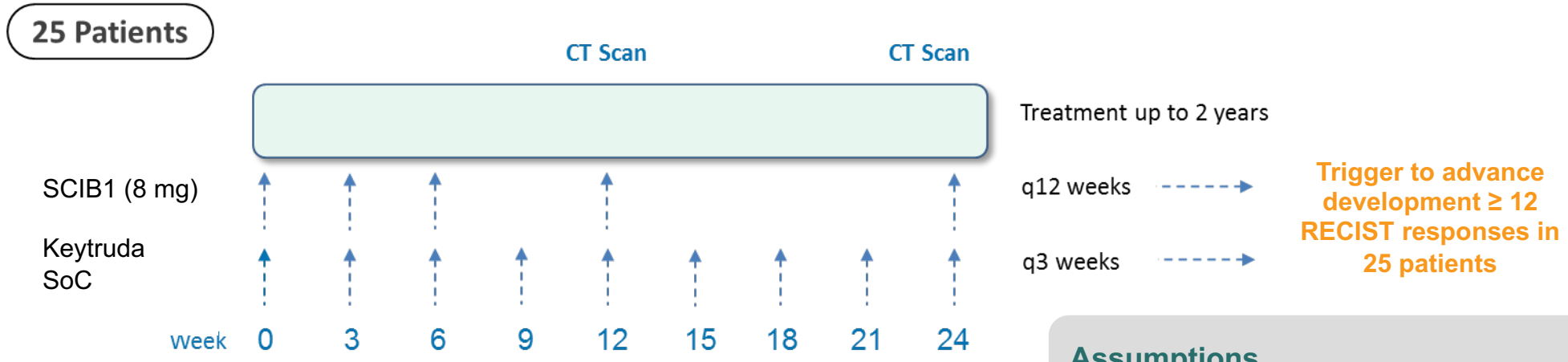
IN A MOUSE MELANOMA MODEL, SURVIVAL RATES WERE SIGNIFICANTLY BOOSTED WHEN ANTI-PD-1 THERAPY WAS COMBINED WITH SCIB1 TREATMENT

- Survival rates for SCIB1 ImmunoBody® monotherapy ≈ anti-PD-1
- Combination therapy resulted in an 85% survival rate
- SCIB1 also upregulates PD-L1 expression and memory response
- Monotherapy viable option for resected melanoma patients



PATIENT POPULATION

- Histologically confirmed, unresectable AJCC stage III or stage IV melanoma
- No prior systemic treatment for advanced disease
- Suitable for treatment with Keytruda (pembrolizumab), with measurable disease
- Part 1 safety run-in (n=6); Part 2 additional 19 patients; total = 25 patients



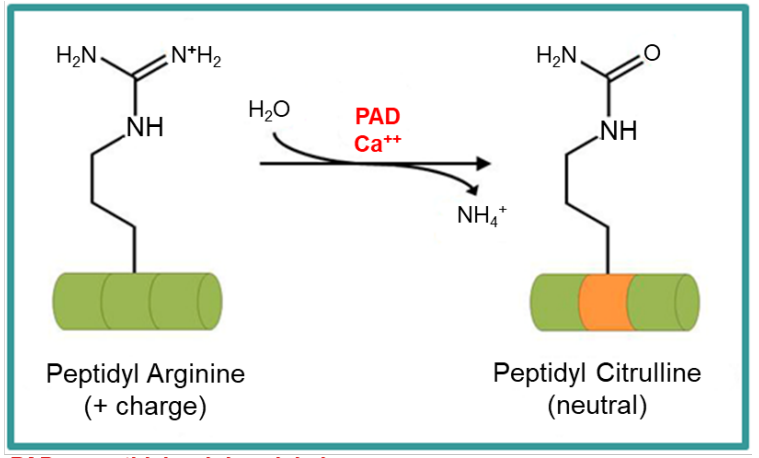
Assumptions

- Response rate to Keytruda = 30%
- Response rate of interest for combination = 55%

Stress-Induced Post-Translational Modifications (siPTM)

- One such modification involves the process of **CITRULLINATION**
  - The alteration of proteins due to enzymatic conversion of arginine residues to citrulline
  - Citrullination occurs as a result of a degradation and 'recycling' process called **autophagy** that is induced in stressed cells, including cancer cells
  - Citrullinated epitopes presented on **MHC class II**
  - Patent awarded in Europe, Japan, China, Australia; some claims allowed in the US and broader claims under review

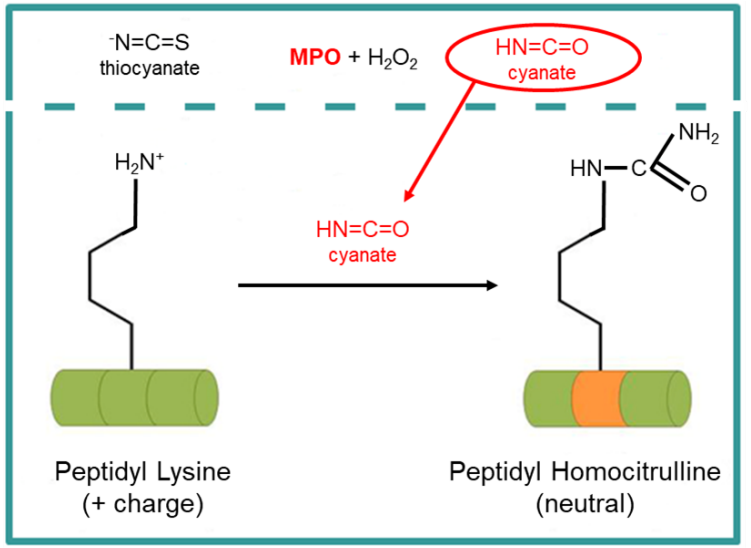
Modi-1



PAD = peptidylarginine deiminase

- Another modification involves the process of **HOMOCITRULLINATION**
  - The alteration of proteins due to conversion of lysine residues to homocitrulline
  - Homocitrullination occurs as a result of MPO released by myeloid-derived suppressor cells (MDSC) which converts thiocyanate to cyanate in the presence of H_2O_2
  - Cyanate diffuses into tumor cells and results in spontaneous homocitrullination of cytoplasmic proteins
  - These proteins are degraded and homocitrullinated epitopes presented on **MHC class II**
  - Patent filed with broad claims in cancer and composition of matter for any use of homocitrullinated peptides

Modi-2

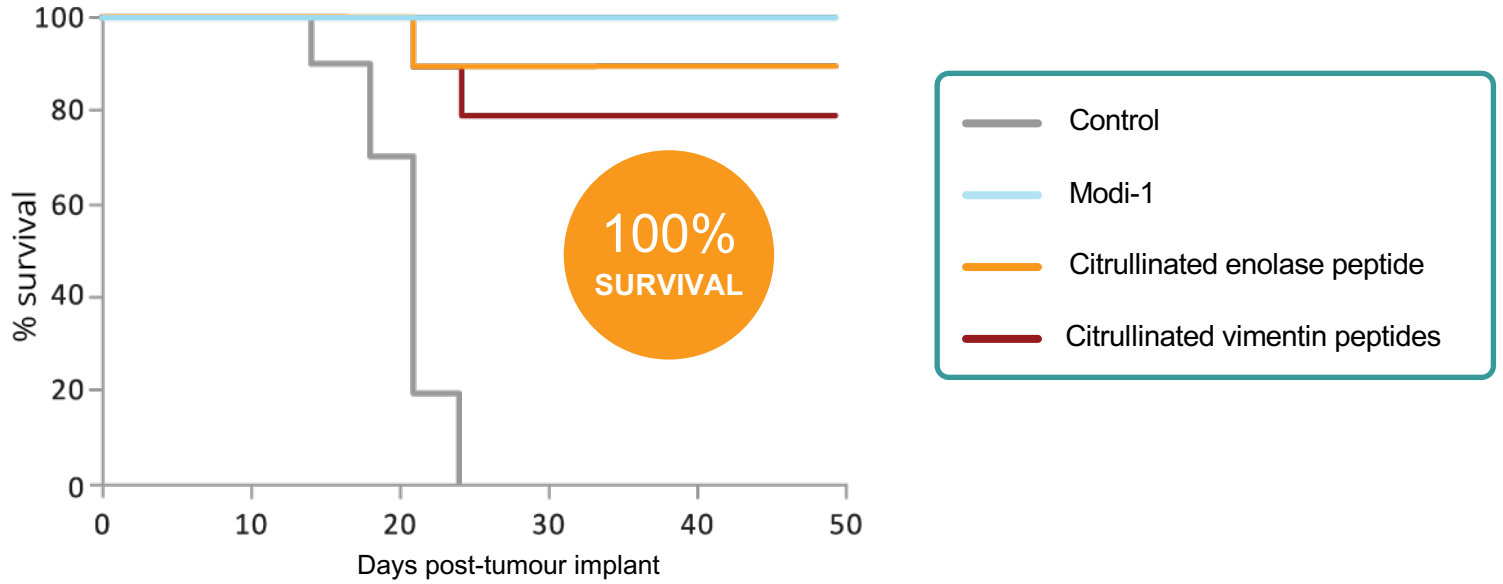


MPO = myeloperoxidase

MODITOPE® LEAD CANDIDATE: Modi-1

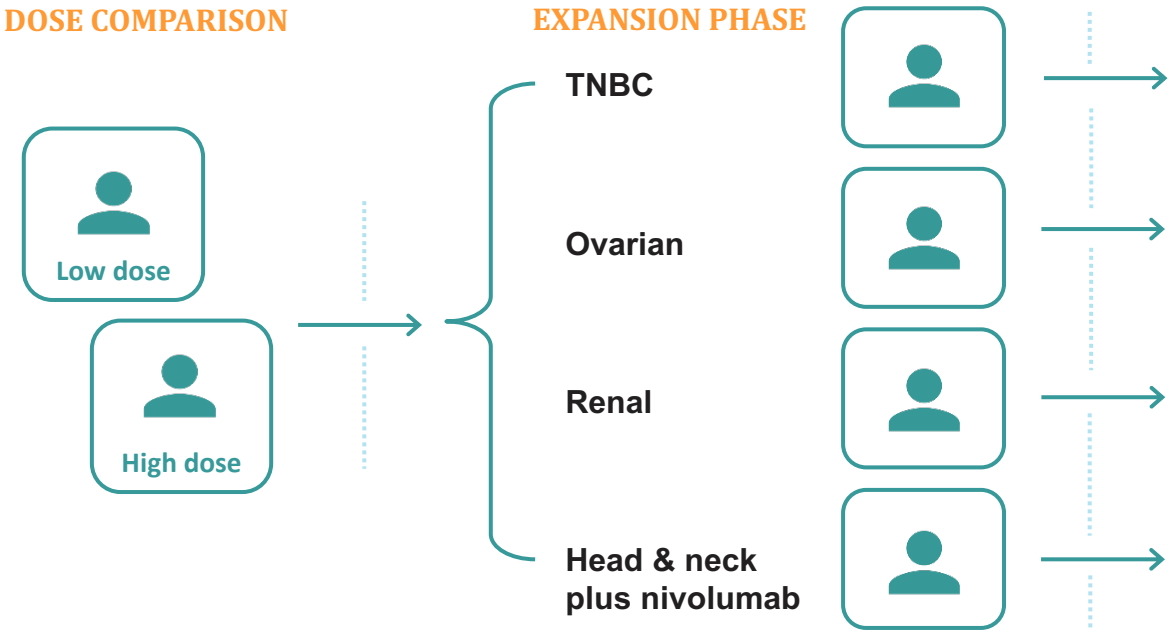
- Consists of:
  - Two citrullinated vimentin peptides (Vim-1 and Vim-2)
  - One citrullinated enolase peptide (Eno-1)

  } Conjugated with Amplivant® adjuvant to boost immune response
- Vimentin and enolase targets are highly expressed in triple negative breast cancer (TNBC), ovarian cancer, renal cancer and head & neck cancer and many other solid tumours with high unmet medical need
- Modi-1 induced potent anti-tumour responses in mice with established melanoma (B16)
- A single immunisation of Modi-1 resulted in a 100% survival rate in animal models



STUDY DESIGN

- Two initial cohorts to explore low and high conjugate doses
- Criteria to expand cohorts: ≥ 30% of patients show an immune response and <2 dose-limiting toxicity (DLT) at selected dose
- Second part of the study will enrol four tumour-specific expansion cohorts
- If selected for expansion, HPV-negative head and neck patients will be treated with nivolumab and Modi-1



Monotherapy cohorts (TNBC, ovarian and renal)

Simon 2-stage* design requires ≥19% of patients to respond for further investigation

Combination therapy (HPV -ve HNSCC)

Simon 2-stage* design requires ≥28% of patients to respond for further investigation

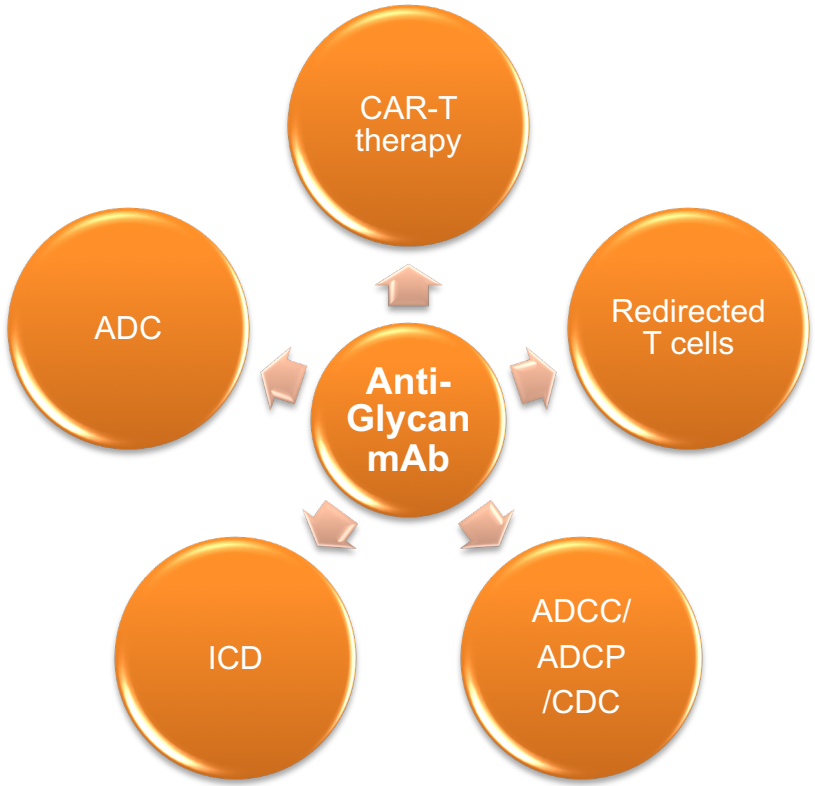
Simon 1989: Optimised 2-stage designs for Phase 2 clinical trials. Controlled clinical trials. Vol 10; 1-10.

- Protocol reviewed by Clinical Advisory Board (Chairman: Prof Robert Coleman)

AvidiMab™ and MABs TARGETING TUMOUR ASSOCIATED GLYCANS (TaG)

Glycosylation is a recognised modulator of the malignant phenotype of cancer cells

- 5 anti-glycan mAbs FG88, FG27, FG129, FL134, FG2811 –unique direct cancer targets
  - Ultraspecific to unique tumour associated glycans (TaG)
  - IgG mAbs with subnanomolar functional affinity
  - Direct cell killing and induce potent ADCC/ADCP and CDC
  - FG2811 recognises and stimulates TSCM –agonist mAb
- AvdiMab™ method to enhance potency – could apply to any mAb
- Rapidly internalise and are good carriers for drugs (ADC)
- Potential targets for redirected T cell and CAR-T therapy



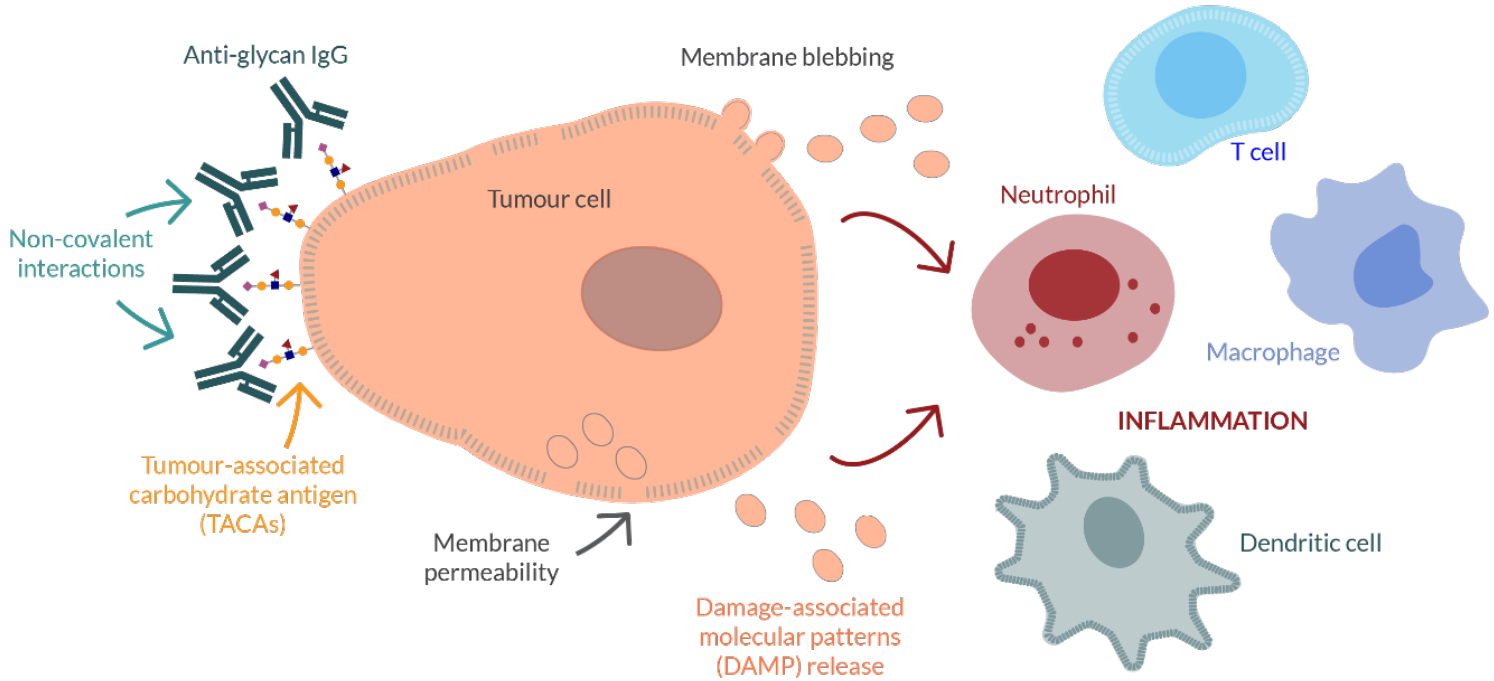
Expression of same glycan on proteins and lipids → multiple approaches to targeting cancer cells

AvidiMab™ Key Features:

- Enhances functional affinity
- Increases direct cell killing
- Improved in vitro and in vivo anti-tumour activity
- Could improve the therapeutic index of any monoclonal antibody
- Patent protected

Increases the avidity of human antibodies by promoting non-covalent Fc-Fc interactions.

This modification promotes the direct tumour cell killing ability of anti-glycan mAbs.



TaG ANTIBODY SUMMARY

mAb	FG27	FG88	FG129	FL133/4	FG2811
Glycan target	Lewis^{y} (ultraspecific)	Lewis$^{a/c/x}$	Sialyl-di-Lewis^{a}	FucGM1	SSEA-4 Stimulates stem cell memory (T_{SCM})
Antigen	Glycolipids & glycoproteins	Glycolipids & glycoproteins	Glycoproteins	Glycolipid	Glycolipid
Tumour targets	Colorectal, Gastric, Pancreatic, Ovarian, Breast	Colorectal, Gastric, Pancreatic, Ovarian, Breast, Lung	Colorectal, Gastric, Pancreatic	Small cell lung cancer	Any solid tumour - recognises Hu/Mse T_{SCMs}
Normal tissue reactivity	Weak on stomach and pancreas	GI tract	Very weak oesophagus	TBD	T_{SCM}
ADC activity	1 nM	10 pM	10 pM	No	NA
Direct killing activity	30-100 nM	2-10 nM	20 nM	TBD	Agonist mAb
Immune mediated killing ADCC/CDC	ADCC:1 nM CDC:5 nM	ADCC:1 nM CDC:1 nM	ADCC:0.1 nM CDC:20 nM	ADCC:2 nM CDC:100 nM	NA
mAb structure	Humanised	Chimeric	Chimeric	Chimeric	Chimeric
Potential fields of use	ICD ADC CAR-T Bispecifics	ICD	ICD ADC CAR-T Bispecifics	CAR-T Bispecifics	In vivo and In vitro T_{SCM} expansion

Broad scope and utility → multiple licensing opportunities

ADC = antibody drug conjugate; ADCC/CDC = antibody-dependent cell-mediated cytotoxicity/complement-dependent cytotoxicity; ICD = immunogenic cell death; CAR-T = chimeric antigen receptor T cells; TBD = to be determined

HIGHLIGHTS FOR CY19

Operational

- **SCIB1 Phase II trial**
  - MHRA approval and initiation of UK arm of study
- **Modi-1 manufacturing**
  - GMP manufacturing and toxicology studies
- **Strengthened team and Clinical Advisory Board**
  - Head of Research and Head of Manufacturing
  - Established Clinical Advisory Board (CAB)
- **Cancer Research UK SCIB2 partnership update**
  - Nano-particle delivery of SCIB2 preclinical results
- **Expanded IP portfolio**
  - EU and US patent grant for protection of Modi-1
- **Expanded utility of AvidiMab and TaG mAbs**
  - Two evaluation agreements for potential partnering transactions

Financial

- **Vulpes investment and Board position**
  - In June, Scancell raised gross proceeds of £3.88m by the issue of 77.6m new ordinary shares to Vulpes Life Sciences Fund
  - Martin Diggle, Co-Founder and Portfolio Manager of Vulpes Investment Management, appointed to the Company's Board of Directors as a Non-Executive Director.

ANTICIPATED NEWSFLOW + MILESTONES

IMMUNOBODY®

SCIB1

- SCIB1/checkpoint inhibitor Phase 2 study in late stage melanoma
  - Activation of additional study centres in UK and US to accelerate patient recruitment and generation of interim clinical data

SCIB2

- CRUK development activities for initiation of SCIB2 Phase 1/2 study for solid tumours

MODITOPE®

Modi-1

- First-In-Human study with Modi-1 in patients with TNBC, ovarian cancer, renal cancer and HNSCC planned to start 2H CY20
- Identification of Modi-specific TCRs in collaboration with BioNTech

Modi-2

- Pre-clinical validation for multiple solid tumour indications
- Extension of patent portfolio

AvidiMab™ / TaG mAbs

- Additional validation data /publications and extension of patent portfolio
- Transition of established research/evaluation agreements to potential partnerships

OUTLOOK

3 PLATFORMS +BROAD PIPELINE+ 5 CORE ACTIVITIES

CLINICAL DATA	▶ Generate meaningful clinical data to address unmet needs: clinical read-outs (SCIB1 Phase 2 & Modi-1 Phase1/2 interim data) anticipated within next 18 months
PIPELINE EXPANSION	▶ Extend utility of Moditope® platform beyond Modi-1 and Modi-2 in association with key industry players e.g., TCRs ▶ Expanded utility and validation of anti-glycan mAbs and AvidiMab platform
TECHNOLOGY PARTNERSHIPS	▶ Evaluate and implement enabling technologies e.g., nano-vesicle delivery (Immunobody®), and adjuvant (Moditope®), to aid and de-risk development
CLINICAL PARTNERSHIPS	▶ Establish relationships with key opinion leaders and clinical networks to ensure utility in clinical practice e.g., CRUK, CAB, and patient advocacy
INDUSTRY PARTNERSHIPS	▶ Explore synergies with large Pharma/Biotech companies in identifying combination therapies for optimal outcomes e.g., checkpoint inhibitors

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